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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,072	06/22/2001	Richard B. Greenwald	213.1090-CIP2	8104

22856 7590 12/31/2003

MUSERLIAN, LUCAS AND MERCANTI, LLP  
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NEW YORK, NY 10016

EXAMINER

DESAI, ANAND U

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 12/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/888,072

Applicant(s)

GREENWALD ET AL.

Examiner

Anand U Desai

Art Unit

1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 December 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 2-4, 6-8, 10 and 12-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 5, 9, 11, 15 and 16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election with traverse of a species directed to claims 1, 5, 9, and 15-16 in Paper filed November 3, 2003 is acknowledged. The traversal is on the ground(s) that the examination of different species is not such as to require a different search. This is not found persuasive because the multiple compounds have different structures and would require a separate examination.

The requirement is still deemed proper and is therefore made FINAL.

Claims 2-4, 6-8, 10, 12-14 have been withdrawn from further consideration because these claims are drawn to non-elected inventions. Claims 1, 5, 9, 11, and 15-16 are under examination.

### ***Priority***

2. Priority is acknowledged for the instant application filed June 22, 2001. This application is a continuation-in-part of U.S. Patent Application No. 09/293,557, now U.S. Patent 6,251,382, which in turn claims the benefit of priority from U.S. Patent Provisional Application Serial No. 60/082,105 filed April 17, 1998.

### ***Specification***

3. The disclosure is objected to because of the following informalities:

The cross-reference to related applications can be updated to include the U.S. Patent number for previous U.S. Patent Application No. 09/293,557.

The specification contains underlined words, such as in vivo on page 1 and Remington's Pharmaceutical Sciences on page 2, “\_” which is normally intended to indicated added matter. See 37 CFR 1.121(b). Suggest removing underline.

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- (b) *Specification other than the claims and listings provided for elsewhere (§ 1.96 and 1.825). —*
- (1) *Amendment by instruction to delete, replace, or add a paragraph.*  
Amendments to the specification, other than the claims and listings provided for elsewhere (§§ 1.96 and 1.825), may be made by submitting:
- (i) An instruction, which unambiguously identifies the location, to delete one or more paragraphs of the specification, replace a deleted paragraph with one or more replacement paragraphs, or add one or more paragraphs;
  - (ii) Any replacement or added paragraph(s) in clean form, that is, without markings to indicate the changes that have been made; and
  - (iii) Another version of any replacement paragraph(s), on one or more pages separate from the amendment, marked up to show all the changes relative to the previous version of the paragraph(s). The changes may be shown by brackets (for deleted matter) or underlining (for added matter), or by any equivalent marking system. A marked up version does not have to be supplied for an added paragraph or a deleted paragraph as it is sufficient to state that a particular paragraph has been added, or deleted.

Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 112***

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5, and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The substituent R<sub>1</sub>, and the variable "x" is undefined in claim 5? In claim 9, the substituents X<sub>5</sub>, Y<sub>15</sub>, R<sub>54</sub>-R<sub>58</sub>, and the letter g are undefined?

#### ***Claim Rejections - 35 USC § 103***

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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7. Claims 1, 5, 9, 11, 15, and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Greenwald et al. U.S. Patent 6,011,042 in view Greenwald et al. J. Med Chem. (1996) 39(10):1938-1940 and Greenwald et al. U.S. Patent 5,965,566. Greenwald et al. (U.S. Patent '042) teach conjugates of aromatic hydroxyl containing compounds, such as camptothecin, with polyalkylene oxide, such as polyethylene glycol (U.S. Patent '042, claims 1, 11, 12, 18, 19; current application, claim 1, 11). Greenwald et al. (U.S. Patent '042) does not teach a 20-O amino acid ester of camptothecin. Greenwald et al. (U.S. Patent '566) teach a biodegradable 20-O amino acid ester of camptothecin (U.S. Patent '566, column 11, lines 30-60, example 30, and claim 30; current application 1, 5, 9, 11). Greenwald et al. (U.S. Patent '566) also teach a method of preparing a biodegradable polymeric prodrug conjugate (U.S. Patent '566, claims 29, 38, and 39; current application, claim 15), and a method of treating mammals with the polymeric prodrug conjugate (U.S. Patent '566, claim 21; current application, claim 16). One would have been motivated to make a 20-O ester of camptothecin because Greenwald et al. (J. Med. Chem) has shown that forming a polyethylene glycol ester with camptothecin at position 20 stabilizes the active lactone ring which is significant for anti-tumor activity (Greenwald, R. et al. J. Med Chem. (1996) 39(10):1938-1940, see last paragraph on page 1938). Therefore, it would have been obvious to the person having ordinary skill in the art to make the biodegradable polymeric prodrug conjugate at the 20-O position of camptothecin to treat mammals (current application, claims 1, 5, 9, 11, 15 and 16).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U Desai whose telephone number is (703) 305-4443. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 4:30 p.m..

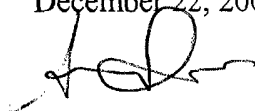
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0198.

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December 22, 2003

A handwritten signature, likely of Christopher S. F. Low, in dark ink.

*Christopher S. F. Low*  
CHRISTOPHER S. F. LOW  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600